

CLAIMS

1. A method of prevention, treatment or alleviation of a fibrotic condition, comprising the step of  
5 administering an effective amount of an antagonist of a C5a receptor to a subject in need of such treatment, in which the antagonist is a peptide or a peptidomimetic compound.

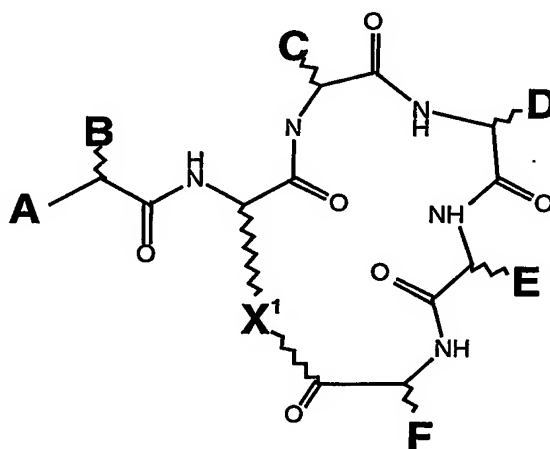
2. A method according to claim 1, in which the antagonist is a cyclic peptide or a cyclic peptidomimetic  
10 compound.

3. A method according to claim 1 or claim 2, in which the inhibitor is a compound which

a) is an antagonist of a G protein-coupled receptor,

15 b) has substantially no agonist activity, and

c) is a cyclic peptide or peptidomimetic compound of formula I



20 where A is H, alkyl, aryl, NH<sub>2</sub>, NH-alkyl, N(alkyl)<sub>2</sub>, NH-aryl, NH-acyl, NH-benzoyl, NHSO<sub>3</sub>, NHSO<sub>2</sub>-alkyl, NHSO<sub>2</sub>-aryl, OH, O-alkyl, or O-aryl;

25 B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-

homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

C is the side chain of a D-, L- or homo-amino acid such as glycine, alanine, leucine, valine, proline, 5 hydroxyproline, or thioproline, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

10 E is a bulky substituent, but is not the side chain of D-tryptophan, L-N-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

15 F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X is  $-(CH_2)_nNH-$  or  $(CH_2)_nS-$ , where n is an integer of from 1 to 4;  $-(CH_2)_2O-$ ;  $-(CH_2)_3O-$ ;  $-(CH_2)_3-$ ;  $-(CH_2)_4-$ ; 20  $-CH_2COCHRNH-$ ; or  $-CH_2-CHCOCHRNH-$ , where R is the side chain of any common or uncommon amino acid.

4. A method according to claim 3, in which n is 2 or 3.

5. A method according to claim 3 or claim 4, in which 25 A is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.

6. A method according to claim 5, in which A is a substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6, or a phenyl or toluyll group.

30 7. A method according to claim 6, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.

8. A method according to any one of claims 3 to 7, in which B is the side chain of L-phenylalanine or L-phenylglycine.

35 9. A method according to any one of claims 3 to 8, in which C is the side chain of glycine, alanine, leucine,

valine, proline, hydroxyproline, or thioproline.

10. A method according to any one of claims 3 to 9, in which D is the side chain of D-Leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine.

11. A method according to any one of claims 3 to 10, in which the antagonist is a compound which has antagonist activity against C5aR, and has no C5a agonist activity.

12. A method according to any one of claims 1 to 11, in which the inhibitor has potent antagonist activity at sub-micromolar concentrations.

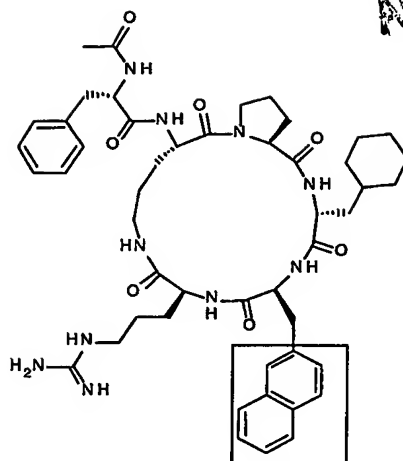
13. A method according to any one of claims 1 to 12, in which the compound has a receptor affinity  $IC_{50} < 25 \mu M$ , and an antagonist potency  $IC_{50} < 1 \mu M$ .

14. A method according to any one of claims 1 to 13, in which the compound is selected from the group consisting of compounds 1 to 6, 10 to 15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33 to 37, 39 to 45, 47 to 50, 52 to 58 and 60 to 70 described in International patent application No. PCT/AU02/01427.

15. A method according to claim 14, in which the compound is AcF[OP-DCha-WR] (PMX53 compound 1), AcF[OP-DPhe-WR] (compound 33), AcF[OP-DCha-FR] (compound 60) or AcF[OP-Dcha-WCit] (compound 45).

16. A method according to claim 15, in which the compound is PMX53, having the formula

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21. A use according to claim 20, in which the fibrotic condition is cardiac fibrosis or pulmonary fibrosis.